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Immobilization of molecular catalysts on electrode surfaces using host–guest interactions

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Abstract

Anchoring molecular catalysts on electrode surfaces combines the high selectivity and activity of molecular systems with the practicality of heterogeneous systems. Molecular catalysts, however, are far less stable than traditional heterogeneous electrocatalysts, and therefore a method to easily replace anchored molecular catalysts that have degraded could make such electrosynthetic systems more attractive. Here, we apply a non-covalent 'click' chemistry approach to reversibly bind molecular electrocatalysts to electrode surfaces through host–guest complexation with surface-anchored cyclodextrins. The host–guest interaction is remarkably strong and enables the flow of electrons between the electrode and the guest catalyst. Electrosynthesis in both organic and aqueous media was demonstrated on metal oxide electrodes, with stability on the order of hours. The catalytic surfaces can be recycled by controlled release of the guest from the host cavities and readsorption of fresh guest.

Molecular electrocatalysts can exhibit surprisingly high activities and selectivities that are unmatched by most heterogeneous catalysts.[1,2] Therefore, the development of robust immobilization strategies for these molecular species on electrode surfaces is of great interest if these molecular catalytic activities and selectivities are to be transferred to more practical heterogeneous electrosynthetic systems,[3] which have already shown promising results for CO_2 reduction, water reduction and water oxidation in the context of storage of renewable energy.[4–6] Over the past decades, many immobilization strategies have been developed,[7] which can be categorized into covalent binding (achieved by adding anchoring groups such as carboxylate to the catalysts),[8] non-covalent binding (pi-stacking on carbon-based electrodes)[9,10] and polymerization-based binding.[11–13] Here, we report a new strategy for surface immobilization of molecular electrocatalysts, which relies on a non-covalent 'click' chemistry approach to bind molecular species in well-defined sites on electrode surfaces.[14]

The binding of electroactive molecular guests into molecular pockets by means of host–guest complex (HGC) formation has previously been studied by several groups, including those of Stoddart and Kaifer,[15] Reinhoudt [16,17] and Huskens.[18] Liu *et al.* reported the HGC-formation on gold surfaces with the C_{60} monoanion as guest, which was found to be electrochemically stable over prolonged durations.[19] Light-induced electron transfer to and from dye molecules bound via the HGC approach was also demonstrated by Freitag and Galoppini.[20,21] The group of Sun demonstrated the use of HGC to improve electron transfer between a molecular catalyst and a dye molecule bound onto TiO_2.[22]

Among the diverse class of host molecules, cyclodextrins, cucurbiturils and calixarenes are the most studied for HGC formation on different surfaces.[23,24] For cyclodextrins, the electron transfer rates between the electrode and guest molecules situated inside the surface-bound hosts have been reported to be on the order of 100 s^{-1}, indicating the potential applicability of these systems for molecular electrocatalysis.[25] It was found that the binding of the guest was not affected by redox processes if the binding units do not undergo oxidation themselves.

Although rapid electron transfer to HGC-bound molecules has been demonstrated, to the best of our knowledge there have been no reports on using this approach to bind molecular catalysts to electrode surfaces, likely because the dynamic HGC formation in solution phase suggests that rapid desorption would occur.[26] We demonstrate, however, that molecular guests bind with surprisingly high stability and show that these surface-bound HGCs are catalytically active. We also show that the binding of the guests is reversible under controlled conditions and exchange of these guests can be achieved. We further demonstrate regeneration of the catalytic activity of the electrodes after re-adsorption of fresh electrocatalytic guests, implying the high stability of the host under operational conditions of the bound catalysts. This study represents a proof of concept for using stable, multi-dentate supramolecular hosts as anchoring moieties for molecular electrocatalyst guests, generating stable and electrocatalytically active surface-bound HGCs in both aqueous and organic solvents.

Results and Discussion

We designed the immobilization system to be as compact as possible, using short tethers to attach the hosts to the electrode surface, ensuring close contact between the electroactive guest and the electrode surface. An aromatic linker was chosen as guest binding unit to facilitate electron transfer to the catalytically active site of the guest. With the compact design, displacement of the guests by water or solvent from the opposite face of the host should be inhibited. Higher binding constants of guests in surface-bound hosts compared to the binding in solution have been reported,[16,27] and the increased binding strength was proposed to be related to further interactions between guest and surface. For hosts with long, flexible chains connecting them to the surface, studies with multi-valent guests showed that HGCs could be stable on a multi-hour time-scale.[28]

Analysis of host–guest complex formation on electrode surfaces

Following our design criteria, we chose to study the per-thiolated derivate of β-cyclodextrin, **1**, as a model for host binding close to the surface (Figure 1 a), as this molecule has been thoroughly studied for its surface-functionalization and surface HGC formation behaviour on gold.[15,19,29,30] As guests, we chose to investigate ruthenium-based electrocatalyst **2**, inspired by the class of molecular catalysts that has very recently been shown to be active for ammonia oxidation in organic electrolytes (ammonia being a promising candidate as a storage medium for renewable hydrogen).[31–34] We also investigated structurally similar ruthenium-based electrocatalyst **3**, a derivate of which we have reported to be active for water oxidation.[35] As a control, fluorescent platinum complex **4** was synthesized, which served as a non-electroactive guest. The complexes used in this study and their crystal structures are given in Figure 1 b-d. The common design feature in the guest metal complexes is the naphthyl substitution on the terpyridine ligand, which was employed as the binding unit of the guests inside the cyclodextrin cavity.

To confirm that binding between the guests and cyclodextrin takes place in solution, fluorescence titrations and NMR experiments were performed (see Supplementary Figures 1 and 2). A 1:1 binding stoichiometry for fluorescent guest **4** with β-CD was determined and a binding constant of $K_{11} = 6.5 \cdot 10^3\ M^{-1}$ was obtained, which is 2-4 times higher than for other naphthyl-based guests with β-CD. [36,37]

The attachment of **1** on gold substrate was investigated by X-ray photoelectron spectroscopy (XPS) (Supplementary Figure 3) and tip-enhanced Raman spectroscopy (TERS) (*vide infra*). The spectra indicated the expected attachment of the cyclodextrin host via the thiol groups, as was evidenced by the loss of the *v*(S-H) Raman band upon adsorption. The surface density of **1** on Au(111) determined by XPS was found to be up to 0.46 nm^{-2}, corresponding to a relatively compact layer of host molecules on the substrate. We note that the maximum coverage of the surface was achieved with dipping times of 3 minutes, with no further increase in **1** surface coverage at longer exposure of the gold substrate (Supplementary Figure 4).

The formation of HGCs with the gold-bound **1** was investigated using TERS, and DFT calculations were performed to gain a better understanding of this system.[38] The optimization of **1** on an Au(111) slab (more details in the Methods section) revealed the expected binding of the host via all seven thiol groups, despite the mismatch in symmetry with the gold substrate (Figure 2 a), and is consistent with the complete loss of the *v*(S-H) band in the TER spectra of **1** on Au (see Figure 3a).

Formation of the HGCs was first computed at the DFT level of theory for all guests in the gas phase (See Supplementary Figures 5, 6 and 7), which gave binding energies between **1** host and the guests of -2.03 eV (guest **4**) and -2.17 eV (guests **2** and **3**). On the Au(111) surface, the binding energies between guests and surface-bound **1** were found to be between -4.31 eV and -4.89 eV, which reveals a dramatic increase in adsorption energy into the cyclodextrin cavity. This large increase in the adsorption energy is related to delocalization of electronic states of the guest molecules and the gold substrate (see Supplementary Figures 8 and 9), which is evidenced by significant mixing of gold and guest orbitals. The strong interactions and delocalization of electronic states indicate that oxidation or reduction of electroactive guests (**2** and **3**) can be easily achieved. However, strong coupling also implies that the diagnostic redox peaks of the guest in cyclic voltammetry (CV) experiments would be absent, similar to the case with graphite-conjugated molecules that lack clear redox peaks in CV experiments.[39] Indeed, we did not observe redox peaks for the ruthenium-based guests bound to **1** on gold at the respective redox potentials found in solution (Supplementary Figure 10), even as a low catalytic current was observed from the HGC of guest **2** with host **1** on dodecanethiol-poisoned gold substrates (Supplementary Figure 11).

The large binding energies obtained from the DFT calculations provide an understanding of the experimentally observed greater stability of the guests bound to the host-functionalized surface versus HGC binding in solution. Thus, conditions need to be developed to actively remove the guests from the surface-bound hosts for recycling purposes. The desorption of guests under competitive HGC formation in solution

has been reported,[28,40] and this strategy was also employed to show that guest binding to the **1** modified gold substrates could be controlled under specific conditions.

Using TERS (Figure 3a), we were able to track the presence of guest **3** on gold functionalized with host **1**. Formation of the HGC on the Au surfaces was visualized by the appearance of an intense Raman fingerprint of the guest between 1000 and 1600 cm^{-1} compared to the moderately strong ν(C-H) band of **1** at 2900 cm^{-1} (cyclodextrins are very weak Raman scatterers). Desorption of the majority of guest was achieved by soaking and sonication of the sample in a concentrated β-CD solution (indicated by the strong decrease in the guest/host Raman band intensity ratio). Re-adsorption of the guest was observed after re-soaking the desorbed sample in a solution of **3**. In a separate experiment, we also showed that guest **4** (Pt complex) can be exchanged for a second guest **2** by initial desorption of **4** using concentrated β-CD solution and subsequent incubation in a solution of guest **2** (Figure 3 b). The exchange was enabled by the release of guest **4** from the surface-bound host cavities during the desorption step and cannot be explained with stronger binding of guest **2** compared to guest **4**, as the reverse exchange (**2** for **4**) is also feasible (Supplementary Figure 12). Interestingly, complete loss of guest signal after the desorption treatment was never observed, which again hints towards the unexpectedly strong interaction between the guest and the **1**-functionalized gold. Raman and TERS measurements of guest **2** revealed a red-shift of the guest's optical absorption maximum upon host–guest binding on the gold surface, which illustrates the shrinking of the HOMO-LUMO gap predicted by the DFT calculations, providing further evidence for the strong coupling between the gold substrate and the guest (Supplementary Figure 13). Direct observation of **1** and the HGCs on Au(111) was attempted by STM, however a clear image could not be obtained despite significant efforts (Supplementary Figure 14).

Studying the electrochemical properties of the HGCs on gold alone was not sufficient to obtain a clear picture of our catalytic system. Gold electrodes are known to undergo surface oxidation,[41] which leads to the desorption of thiol-based adsorbates.[42,43] Furthermore, the relatively low surface area and high background

activities of gold for many catalytic processes make the analysis of catalytically active adsorbates very difficult.[44]

To address these issues and to compliment the array of available analytical techniques to study the surface-bound HGCs, metal oxide (MO) substrates were used, specifically indium tin oxide (ITO), zirconium dioxide (ZrO_2), and titanium dioxide (TiO_2). As these materials have similar properties in terms of surface-adsorption chemistry,[45] the choice of substrate can be tailored to the application of analytical technique (ITO for electrochemical measurements, ZrO_2 for fluorescence and IR, and TiO_2 for solid state NMR). Furthermore, by preparing mesoporous layers of the MOs, higher surface areas are easily accessible, allowing for the use of further spectroscopic methods and simplifying the analysis of electrochemical data.

To transfer the HGC chemistry from the gold to the MO substrates, two strategies were employed: direct introduction of multiple suitable binding groups, geminal bisphosphonates,[46] to the host scaffold (host **5**, see Figure 1) or pre-functionalization of the MO substrates with propiolic acid and subsequent thiol-yne click chemistry on the surface.[47] Both strategies are schematically shown in Supplementary Figure 15. The host molecules on MO surfaces are slightly further away from the surface, perhaps leading to decreased electronic coupling of the guests with the surface.

Surface binding of the CD hosts was analysed by IR spectroscopy, XPS and solid state NMR (Supplementary Figures 16, 17 and 18). Furthermore, impedance spectroscopy revealed the increased charge-transfer resistance after binding of host **5** to an ITO electrode, which is in accordance with previous observations on gold electrodes (Supplementary Figure 19).[29] Submersion of the host-functionalized electrodes into guest solutions led to the formation of surface-bound HGCs accompanied by physisorbed guest species. The presence of the guests on the surface could be clearly determined by various spectroscopic methods and by electrochemical measurements (Supplementary Figures 20, 21, 22 and 23). Removal of physisorbed species was achieved by treatment of the samples with dilute acetic acid in methanol, as was determined by the loss of guest fluorescence signal from a physisorbed sample on ZrO_2 (Supplementary Figure 24)). Formation of the

host–guest complexes could also be inferred from the cyclic voltammetry experiments: whereas physisorbed guests rapidly desorb after a few cycles, redox-features of the HGCs could be observed even after repeated cycling (Supplementary Figure 25). A binding constant for HGC formation of guest **3** with host **5** on ZrO_2 of $K_{11}^{surf} = 3.3 \cdot 10^5\ M^{-1}$ was calculated based on a Langmuir-type model (Supplementary Figure 26).

Exposing mesoporous ZrO_2 substrates with HGC-bound guests to the desorption conditions used for the gold (with heating of the solution instead of sonication, to preserve the mesoporous substrate), the removal of guests from the surface could be tracked by fluorescence spectroscopy. The same reversible desorption and re-adsorption of different guests (as was shown for the gold electrode using TERS) indicates that the surface can be modified without degrading the surface-bound hosts (Supplementary Figure 27).

Catalysis using host–guest complex bound molecular electrocatalysts

Guest **2** –designed as a molecular ammonia oxidation catalyst and equipped with a naphthyl binding group– shows the expected homogeneous phase catalytic activity for NH_3 oxidation in THF solution around its first oxidation potential (Figure 4 a). A sample with HGC-bound **2** was then tested under the same conditions and also showed a clear onset of catalysis at the same potential as in solution (around -0.1 V vs. Fc/Fc^+, Figure 4 b). The control samples with non-active guest **4** showed a much later onset of NH_3 oxidation (taking place directly on the electrode surface), and physisorbed catalyst led to lower current with a rapid loss of activity during operation (Supplementary Figure 28).

The stability of the HGC-bound electrocatalyst **2** under operation was analysed by chronoamperometry, revealing a slow decrease in current to roughly 70 % of the initial value over 30 minutes (Figure 4 c), with significantly higher currents observed than for physisorbed **2** without host present (Supplementary Figure 29). Re-adsorption of fresh **2** regenerated the catalytic activity of the electrode, which clearly indicates that the host molecules on the electrode surface are intact and can be used to bind fresh catalyst guests. The decrease of current could either be due to slow desorption of the guests or degradation of the HGC-bound

catalyst. Nevertheless, these results show that our immobilization strategy of molecular electrocatalysts using HGCs can be employed to bind active catalysts to electrodes. Moreover, this strategy was effectively used in organic electrolytes, which is notable considering the general competition for occupying the host cavity between guests and solvent molecules.[48,49] This observation underlines the strong adsorption interaction between the guest molecules and the surface bound hosts. Additional soaking experiments of the HGC in organic solvents used in electrochemical catalysis revealed hours of HGC stability in methanol, acetonitrile, dichloromethane and toluene, supporting the observation of unusually stable binding on the surface (Supplementary Figures 30 and 31).

Electrochemical water oxidation was also attempted using guest **3**, which was shown to be active (though sluggish) for this reaction in solution (Supplementary Figure 32). Unfortunately, we could not observe an unambiguous catalytic response for water oxidation versus the background. To nevertheless confirm the activity of HGC-bound guests, we were able to demonstrate catalytic oxidation of a water-soluble phosphine to the corresponding phosphine oxide with HGC-bound **3** on ITO as a model reaction (Supplementary Figure 33). This system also showed similar stability as the case for NH_3 oxidation in organic media. Regeneration of catalytic activity upon readsorption of **3** indicates the robustness of the host on the surface (Supplementary Figure 34).

To confirm that the host is stable during electrocatalysis, we analysed host **5**-functionalized ITO substrates before and after electrochemical measurements (with HGC-bound guest **2**). We observed no peak shifts or decreased intensities for the carbon, phosphorus or sulfur signals pertaining to host **5** between the two measurements (Figure 5) indicating that there is no oxidation of the host structure. To demonstrate the stability also under challenging conditions for most classically anchored catalysts, CV cycling at pH 10 under strong oxidative bias was performed (Supplementary Figure 35), showing only a slow decrease of the guest redox features. Analysis of the sample surface by XPS showed a modest decrease of carbon, sulfur and phosphorus related to surface-bound **5** (Supplementary Figure 36), indicating that the majority of the surface

binding sites remained stable under such harsh conditions on the order of hours. The stability of host **5** under catalytic conditions implies the potential use of this immobilization strategy for different molecular electrocatalysts, with the option of electrode recycling. This also implies that the stability of the anchoring group for surface binding can be decoupled from catalyst design and separately optimized on the host, which presents a promising new approach to developing and improving new ways of coupling molecular electrocatalysts with different electrode surfaces.

Conclusion

Host–guest complex formation on electrode surfaces can be used to immobilize molecular electrocatalysts. A detailed study on the formation of such HGCs on gold, along with DFT calculations, shows a strong binding of the guests to the surface-bound cyclodextrin hosts. By demonstrating the catalytic activity of HGC-bound guests in both organic and aqueous electrolyte, our experiments show the versatility of using this approach to immobilize different electrocatalytic guests for operation in different chemical environments. The high stability of the host structures on the electrode surface allows for regeneration of the electrodes by re-adsorption of fresh catalyst guests, which overcomes one of the largest challenges in immobilized molecular electrocatalysis: the electrodes can be reused even when the catalyst molecules have degraded.

Our work sets the basis for the use of HGC chemistry for catalyst immobilization. Future research efforts focusing on the preparation of new host structures and families, expanding the scope of the catalytic reactions and understanding and improving the control over the interactions between guest, host and surface will allow for this immobilization strategy to be used for many different applications.

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Author Contributions

L.S. and S.D.T conceived and the project. L.S. performed synthesis, electrochemical and catalytic experiments. I.T. assisted with synthesis and electrochemical experiments. J.S. and R.Z. conducted and evaluated TERS experiments. M.T. and J.O. conducted and evaluated XPS and STM experiments. O.B. measured and refined crystal structures. G.T., C.C., F.B.N and M.I. designed, conducted and evaluated calculations. L.S. and S.D.T wrote the manuscript. All authors contributed to discuss the results and revise the manuscript.

Competing Interests

The authors declare no competing interest.

Figure Legends

Figure 1. Chemical structures of host and guest molecules

Structures of the main compounds used in this paper: a) host **1** (thiolated cyclodextrin) and host **5** (bisphosphonated cyclodextrin), along with a depiction of the host cavity; b) guest **2** c) guest **3** d) guest **4**. The crystal structures of guests are displayed showing the 50 % thermal ellipsoids. Solvent and counterions (PF_6^- for guests **2** and **3**; ClO_4^- for guest **4**) are omitted for clarity. Carbon, nitrogen, oxygen, sulfur, ruthenium, platinum and fluorine atoms are depicted as brown, blue, red, yellow, orange, grey and pink, respectively.

Figure 2. Calculated host and host–guest structures on gold

DFT optimized binding structure of 1 on gold in a) plan view and b) side view, showing each thiol group bound to gold in a unique binding geometry. c), d) and e) The optimized structures of HGC bound metal guests **2**, **3** and **4**, respectively, on gold show the guests bound tightly into the host cavity very close to the surface of the electrode, with the catalytically active site (for guests **2** and **3**) above the top face of the host.

Figure 3. Surface analysis of HGCs by TERS

Regeneration and exchange of the catalysts on the host-functionalized Au surface. a) The binding of **1** to Au via all seven thiolate groups is confirmed by the complete absence of the S-H stretching vibration in the TERS spectrum I of **1**-functionalized gold. Reversible adsorption and desorption of **3** on host-functionalized gold is reflected in the varying intensity of the peaks at 1000-1600 cm^{-1} in spectra II-IV. The spectra are normalized with respect to the C-H stretching band of **1** at 2900 cm^{-1} (highlighted in green). b) Desorption and subsequent exchange of **4** by **2** on host-functionalized gold is confirmed by the shift of the ring breathing modes (RBM) of the metal-coordinated pyridyl rings from 1050 cm^{-1} for Pt toward 1030 cm^{-1} for Ru (highlighted in blue). The

incomplete desorption of **4** is reflected in the residual intensity of **4** in spectrum II and in the mixed signals of **4** and **2** in spectrum III.

Figure 4. Electrocatalytic ammonia oxidation by HGCs

Electrocatalytic oxidation of NH_3 in THF solution. a) CV scan under homogeneous reaction conditions using an ITO working electrode in NH_3-saturated THF solution (0.2 M $TBAPF_6$ and 0.1 M NH_4PF_6 as conducting salt and proton source; 10 mV/s scan rate). Without catalyst (black) shows low activity. For a 0.1 mM solution of guest **2** in the absence of NH_3, the Ru(II)/Ru(III) redox peak is observed (green). Upon addition of ammonia, a catalytic onset for ammonia oxidation is observed at the Ru(II)/Ru(III) oxidation potential (magenta). b) CV scans of HGC-bound guests **2** (magenta) and **4** (black) with host **5** on mesoporous ITO show the same catalytic behaviour in the presence of the ruthenium catalyst, with onset at the Ru(II)/Ru(III) oxidation potential measured for HGC-bound **2** without NH_3 (green). The conditions are the same as for (a). c) Chronoamperometry at 0.08 V vs Fc/Fc^+ using host **5**-bound catalyst guests **2** and **4** (the latter as a non-catalytically active reference). Readsorption of guest **2** after 30 minutes of catalysis into the host-functionalized electrodes leads to complete regeneration of catalytic activity.

Figure 5. XPS surface analysis demonstrates host stability

XP spectra of ITO electrodes functionalized with host **5** and HGC-bound guest **2** before and after electrocatalytic measurements (NH_3 oxidation in THF solution). a) C1s spectra. b) P2p spectra. c) S2p spectra. For S2p and P2p, no difference between the sample before and after electrocatalysis is observed, showing no change in oxidation state or decrease in surface coverage for either of the elements. In the case of C1s, a decrease in signal intensity is only observed for the peak at 285 eV which is attributed to adventitious carbon,

while the signal from host C-O carbon species remains unchanged. Overall the data indicate that no degradation of the host takes place under operating conditions.

Methods

Host-functionalization of gold substrates: Gold substrates were used either as prepared (directly after deposition of the gold layer) or cleaned in an O_2 plasma before functionalization. Compound **1** was attached to the gold by soaking the substrates in a solution of **1** (0.1 mM) prepared with either DMSO or DMF. Although adsorption was found to take place in less than 5 minutes, the substrates were soaked for 1 h. The substrates were then soaked in pure solvent (5 minutes), MeOH (5 min) and dried under a stream of N_2. The host-functionalized gold was used immediately or dipped in guest solutions very soon after preparation.

Host-functionalization of metal oxide substrates

Two-step procedure for binding of host 1: The metal oxide substrate was dipped in a solution of propiolic acid (10 µl in 10 ml MeCN) for 30 min. After this, the substrates were dipped in pure MeCN for 5 min to remove excess propiolic acid, then dried under a stream of N_2. The samples were subsequently immersed in a solution of **1** (0.7 mM) in DMF (10 ml) containing NEt_3 (20 µl) for 1 h. The substrates were then soaked in pure DMF (15 ml, 5 min), pure MeOH (10 ml, 5 min) and finally dried under a stream of N_2.

Direct binding procedure for host 5: The salt form of **5** was dissolved in H_2O to give a 0.1 mM solution, to which was added 1 v% of 1 M H_2SO_4, resulting in a pH 2 solution. The metal oxide substrate was then immersed in this solution for 1 h, after which it was placed in pure H_2O (15 ml, 5 min) and MeOH (10 ml, 5 min). The samples were then dried under a stream of N_2.

Guest functionalization of substrates: The appropriate substrates were immersed in a solution of the guest in MeOH (0.05 – 0.1 mM) for 1 h, after which they were soaked in pure MeOH twice (5 minutes each). The substrates were then dried under a stream of N_2. HGC formation was easily observed by eye on mesoporous substrates due to coloration of the films.

Electrochemical measurements

The details for electrochemical measurements are noted in the captions of each Figure containing electrochemical data. For the measurements, BioLogic sp-50, sp-200 or sp-300 instruments were used.

Experiments performed in water were measured against an aqueous Ag/AgCl electrode in saturated KCl. For measurements in organic electrolyte, an organic Ag/AgCl reference electrode was fabricated in a custom-made cell using an etched silver wire (1 M HCl, 2 min, 1.0 V vs Ag/AgCl) and a 0.2 M solution of tetrabutylammonium chloride in dry acetonitrile. This electrode was referenced against ferrocene before and after electrochemical measurements, with $E_{Fc/Fc+}$ = 0.98 V vs Ag/$AgCl_{org}$. Measurements in organic electrolytes were performed under exclusion of oxygen and water. Aqueous electrochemical experiments were performed under nitrogen with N_2-sparged solutions, with the exception of impedance measurements and stability measurements at pH 10, which were performed under ambient conditions.

For measurements in solution, a 1 cm x 2.5 cm piece of FTO on glass (cleaned by sonication in acetone, Deconex solution, water and EtOH for 10 minutes each) was used as the working electrode, submersed by ca. 1 cm (giving a rough geometric electrode surface area of 1 cm^2).

Scan rates of 20, 50, 100 or 500 mV/s were typically used. Voltages reported versus the reversible hydrogen electrode (RHE) were obtained by converting the potentials measured with the Ag/AgCl electrode using the Nernst equation, according to equation 1:

$$E_{RHE} = E_{\frac{Ag}{AgCl}} + 0.059 \cdot pH + E^0_{\frac{Ag}{AgCl}} \quad (1)$$

X-ray photoelectron spectroscopy

XPS measurements were conducted in a modified VG ESCALAB 220 UHV system with a base pressure of 2.10^{-10} mbar. The sample was irradiated with non-monochromatized Mg-Kα X-rays with a photon energy of hv=1253.6 eV and photoelectrons were measured at normal emission. The energy scale was calibrated as described by Seah.[50]

Coverage Analysis

In order to estimate the coverage of 6S-B-CD molecules on Au surfaces, the photoemission intensity of S2p (I_S) was measured and referenced against the intensity of Ag3p$_{3/2}$ (I_{Ag}) emission from a polycrystalline silver sample measured with the same photon flux and sampling area. This method reduces the model dependence of XPS quantitative analysis and was used successfully by Zabka et al.[51] The sulfur signal I_S is attenuated by a factor $e^{-d_{CD}/(\lambda_{CD}(E_{Kin}^{S2p}).cos\theta)}$, where $d_{CD} \sim 7.8$ Å is the thickness of cyclodextrin, θ is the electron emission angle with respect to surface normal, and $\lambda_{CD}(E_{Kin}^{S2p})$ is the inelastic mean free path of S2p photoelectrons in cyclodextrin at the measured kinetic energy as calculated with the Tanuma-Powell-Penn (TPP-2M) equation.[52] Following Zabka et al.[51] the number of sulfur atoms per unit area N_S^{Surf} can be obtained as

$$N_S^{Surf} = \frac{I_S}{\sigma_S.e^{-d_{CD}/(\lambda_{CD}(E_{Kin}^{S2p}).cos\theta)}} . \frac{\sigma_{Ag}.n_{Ag}.\lambda_{Ag}(E_{Kin}^{Ag3p_{3/2}}).cos\theta}{I_{Ag}} \quad (2)$$

where σ_S, σ_{Ag} are photoionization cross sections for S2p and Ag3p$_{3/2}$ core levels,[53] respectively. $n_{Ag} = 58.7\ nm^{-3}$ is the density of silver atoms, and $\lambda_{Ag}(E_{Kin}^{Ag3p_{3/2}})$ is the inelastic mean-free path of Ag3p$_{3/2}$ photoelectrons in Ag. In order to give a fractional monolayer coverage, a hexagonal close packed structure is assumed for the surface unit cell of a complete monolayer of 6S-B-CD molecules (see Supplementary Figure 4). According to this model a full coverage (i.e. 7 sulfur atoms in the molecular surface unit cell) yields $N_S^{Surf,full} = \frac{7}{A} = 2.8\ nm^{-2}$. Finally, the fractional coverage can be calculated by $\varphi = N_S^{Surf}/N_S^{Surf,full}$.

Tip-enhanced Raman spectroscopy

Top–illumination TERS was performed with Ag tips and Au substrates, forming a gap plasmon between the substrate and the tip. We used a scanning tunneling microscope (STM; Ntegra Spectra Upright, NT-MDT), equipped with a 0.7 NA 100× objective (Mitutoyo), coupled to a Raman spectrometer (Solar T-II, NT-MDT) with a CCD (Newton 971 UVB, Andor) thermoelectrically cooled to -85 ℃. The STM was operated in constant current mode. Low bias voltage (0.1 V applied to the sample) was used to avoid injection of tunneling

electrons into the investigated molecules. The laser beam was focused on the tip-sample junction, and plasmon-enhanced Raman spectra were collected from the molecules residing in the plasmonic hot spot under the tip.

TERS tips were obtained by electrochemical etching of Ag wire (0.25 mm diameter, 99.9995%, Alfa Aesar) in a hot solution (20 vol%) of perchloric acid (70%, VWR) in ethanol (absolute, Fluka). A Pt ring counter electrode (0.5 mm wire, 1 cm ring diameter, 99.997%, Alfa Aesar) was dipped below the surface of the etching solution. The Ag wire was dipped 2 mm into the solution, at the center of the Pt counter electrode. In order to ensure the sharpness of the tips, the etching voltage of 10 V was cut off shortly before the end of the process by an automated circuit detecting a high gradient of the current. Following the etching, the tips were rinsed with MilliQ water and ethanol.

TER spectra were acquired on square grids with 100-225 pixels (from 10 × 10 to 15 × 15 pixels), with laser illumination at 632.8 nm (HeNe laser) and laser power between 1.4 and 21.2 kW/cm^2. The integration time was 1–3 s. This approach, along with the low laser power applied, enabled the minimization of photoinduced sample damage. The TER spectra presented in Figures 3 and Supplementary Figures 12 and 13 are average spectra accumulated over grids of pixels.

DFT calculations: Optimized structures, energies and electronic properties were obtained by DFT simulations using the Gaussian and plane waves (GPW) method as implemented in the CP2K program package.[38] Valence electrons were treated explicitly, while norm-conserving Goedecker-Teter-Hutter (GTH) pseudo potentials [54] were used to describe the interactions between the valence electrons and the atomic cores. The molecular orbitals were expanded in double-zeta valence plus polarization (DZVP) basis sets,[55] which were optimized on molecular geometries (Mol-Opt method). A cutoff of 600 Ry was used for the auxiliary plane wave basis set. The geometry optimizations were performed using the Perdew-Burke-Enzerhof (PBE) exchange-correlation functional.[56] Dispersion interactions were included via the nonlocal electron correlation scheme conceived by

Vydrov and Van Voorhis, in the revised form (rVV10) proposed by Sabatini et al. [57] The electronic densities of states were refined at the hybrid functional level of theory, specifically the HSE06.[58]

The HGCs on gold were simulated using an Au(111) slab model with four 9x9 layers and periodic boundary conditions were applied. The adsorption energies of the host–guest complexes in the gas phase were computed by comparing the energy of the optimized complex and the energies of the individually optimized CD and catalyst

$$E_{Ads} = E_{HG,gas} - \left(E_{host,gas} + E_{guest,gas}\right).$$

The adsorption energy of the guest into the anchored CD on Au(111) were computer as

$$E_{Ads} = E_{HG,Au} - \left(E_{host,Au} + E_{guest,gas}\right).$$

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Data Availability

The source data for the figures in the main text and Supplementary Information document are available on DataDryad (doi: 10.5061/dryad.6t1g1jwxr). Crystallographic data for the structures reported in this Article have been deposited at the Cambridge Crystallographic Data Centre, under deposition numbers CCDC 1996726 (**2**), 1996727 (**3**) and 1976728 (**4**). Copies of the data can be obtained free of charge via https://www.ccdc.cam.ac.uk/structures/.